

CLAIMS

What is claimed is:

1. A compound selected from the group consisting of 4-aza-4-(2-methyl-2-(nitrosothio)propyl)tricyclo(5.2.1.0<2,6>)dec-8-ene-3,5-dione or a pharmaceutically acceptable salt thereof; and 4-(1-methyl-1-(nitrosothio)ethyl)-1,3-oxazolidin-2-one or a pharmaceutically acceptable salt thereof.
- 5 2. A composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier.
3. The composition of claim 3, further comprising at least one penetration enhancer, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase, or a pharmaceutically acceptable salt thereof and/or at least one vasoactive agent or a pharmaceutically acceptable salt thereof.
4. The composition of claim 3, wherein the at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase
10 is an S-nitrosothiol.
5. The composition of claim 4, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-N-acetylpenicillamine, S-nitroso-homocysteine, S-nitroso-cysteine, S-nitroso-glutathione or S-nitroso-cysteinyl-glycine.
6. The composition of claim 5, wherein the S-nitrosothiol is S-nitroso-glutathione.
- 15 7. The composition of claim 4, wherein the S-nitrosothiol is:
 - (i) $\text{HS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{SNO}$;
 - (ii) $\text{ONS}(\text{C}(\text{R}_e)(\text{R}_f))_m\text{R}_e$; and
 - (iii) $\text{H}_2\text{N}-\text{CH}(\text{CO}_2\text{H})-(\text{CH}_2)_m-\text{C}(\text{O})\text{NH}-\text{CH}(\text{CH}_2\text{SNO})-\text{C}(\text{O})\text{NH}-\text{CH}_2-\text{CO}_2\text{H}$;wherein m is an integer from 2 to 20; R_e and R_f are each independently a hydrogen, an
20 alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, an alkylaryl, a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cycloalkylthio, a cycloalkenyl, a cyano, an aminoalkyl, an
25 aminoaryl, an aryl, an arylalkyl, an alkylaryl, a carboxamido, a alkylcarboxamido, an

arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, a carbamate, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarbonyl, an arylcarbonyl, an ester, a carboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, a sulfonic ester, a urea, a phosphoryl, a nitro, -T-Q, or $-(C(R_e)(R_f))_k-T-Q$, or R_e and R_f taken together with the carbon atom to which they are attached form a carbonyl, a methanthial, a heterocyclic ring, a cycloalkyl group or a bridged cycloalkyl group; Q is -NO or -NO₂; and T is independently a covalent bond, a carbonyl, an oxygen, -S(O)_o- or -N(R_a)R_i-, wherein o is an integer from 0 to 2, R_a is a lone pair of electrons, a hydrogen or an alkyl group; R_i is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an aryl carboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylaryl, an alkylsulfinyl, an alkylsulfonyl, an arylsulfinyl, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an amino alkyl, an amino aryl, -CH₂-C(T-Q)(R_e)(R_f), or -(N₂O₂-)•M⁺, wherein M⁺ is an organic or inorganic cation; with the proviso that when R_i is -CH₂-C(T-Q)(R_e)(R_f) or -(N₂O₂-)•M⁺; then "-T-Q" can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group.

8. The composition of claim 3, wherein the at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase is:

- (i) a compound that comprises at least one ON-O-, ON-N- or ON-C- group;
- (ii) a compound that comprises at least one O₂N-O-, O₂N-N-, O₂N-S- or -O₂N-C- group;
- (iii) a N-oxo-N-nitrosoamine having the formula: R¹R²N-N(O-M⁺)-NO, wherein R¹ and R² are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M⁺ is an organic or inorganic cation.

9. The composition of claim 8, wherein the compound comprising at least one ON-O-, ON-N- or ON-C- group is an ON-O-polypeptide, an ON-N-polypeptide, an ON-C-polypeptide, an ON-O-amino acid, an ON-N-amino acid, an ON-C-amino acid, an ON-O-sugar, an ON-N-sugar, an ON-C-sugar, an ON-O-oligonucleotide, an ON-N-oligonucleotide, an ON-C-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, saturated or unsaturated,

substituted or unsubstituted, aliphatic or aromatic ON-N-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-C-hydrocarbon, an ON-O-heterocyclic compound, an ON-N-heterocyclic compound or a ON-C-heterocyclic compound.

5 10. The composition of claim 8, wherein compound comprising at least one O₂N-O-, O₂N-N-, O₂N-S- or O₂N-C- group is an O₂N-O-polypeptide, an O₂N-N-polypeptide, an O₂N-S-polypeptide, an O₂N-C-polypeptide, an O₂N-O-amino acid, O₂N-N-amino acid, O₂N-S-amino acid, an O₂N-C-amino acid, an O₂N-O-sugar, an O₂N-N-sugar, O₂N-S-sugar, an O₂N-C-sugar, an O₂N-O-oligonucleotide, an O₂N-N-oligonucleotide, an O₂N-S oligonucleotide, an O₂N-C-
10 oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-O-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-N-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-S-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O₂N-C-
15 hydrocarbon, an O₂N-O-heterocyclic compound, an O₂N-N-heterocyclic compound, an O₂N-S-heterocyclic compound or an O₂N-C-heterocyclic compound.

 11. The composition of claim 3, wherein the at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase is
20 L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosated N-hydroxy-L-arginine, nitrosylated N-hydroxy-L-arginine, citrulline, ornithine, glutamine, lysine, polypeptides comprising at least one of these amino acids or inhibitors of the enzyme arginase.

 12. The composition of claim 3, wherein the at least one compound that donates,
25 transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase is a NONOate.

 13. The composition of claim 3, wherein the vasoactive agent is a potassium channel activator, a calcium channel blocker, an α -adrenergic receptor antagonist, a β -blocker, a
30 phosphodiesterase inhibitor, adenosine, an ergot alkaloid, a vasoactive intestinal peptide, a prostaglandin, a dopamine agonist, an opioid antagonist, an endothelin antagonist, a thromboxane inhibitor or a mixture thereof.

14. The composition of claim 3, wherein the penetration enhancer is dimethylsulfoxide, dimethyl formamide, N,N-dimethylacetamide, decylmethylsulfoxide, polyethylene glycol monolaurate, polyethyleneglycol, glycerol monolaurate, lecithin, a 1-substituted azacycloheptan-2-one, a lower alkanol, a C₆ to C₂₀-hydrocarbyl substituted 1,3-dioxane, a C₆ to C₂₀-hydrocarbyl substituted 1,3-dioxolane or a C₆ to C₂₀-hydrocarbyl substituted acetal, an alkonate, a glyceride, a surfactant, or a mixture thereof.

15. The composition of claim 14, wherein the glyceride is a mono glyceride, a diglyceride, a triglycerides, a polyglycolyzed glyceride or a mixture thereof.

16. The composition of claim 15, wherein the glyceride is a mixture of caprylic triglycerides and capric triglycerides, a decanoly triglyceride, an octanoyl triglyceride, a C₈-C₁₂ triglyceride, a saturated polyglycolyzed glyceride, a glyceryl caprylate/caprate and PEG-8 (polyethylene glycol) caprylate/caprate complex, a unsaturated polyglycolyzed glyceride, an apricot kernel oil PEG-6 complex, an almond oil PEG-6 complex, a peanut oil PEG-6 complex, an olive oil PEG-6 complex, a corn oil PEG-6 complex, an ethoxylated glyceride, a glyceryl caprylate/caprate PEG-4 complex, or a mixture thereof.

17. A method for treating a sexual dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 2.

18. The method of claim 17, wherein the patient is female.

19. The method of claim 17, wherein the patient is male.

20. The method of claim 17, wherein the composition is administered orally, buccally, topically, by injection, by inhalation or by transurethral application.

21. The method of claim 20, wherein the composition is administered orally as a solid or liquid dose.

22. The method of claim 17, further comprising administering at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or the at least one vasoactive agent

23. The method of claim 22, wherein the at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and the at least one vasoactive agent are administered separately.

24. The method of claim 22, wherein the at least one compound that donates, transfers

or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and the at least one vasoactive agent are administered in the form of a composition.

25. A kit comprising at least one compound of claim 1.

26. The kit of claim 25, further comprising at least one penetration enhancer, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one vasoactive agent.

27. A compound selected from the group consisting of 4-aza-4-(2-methyl-2-sulfanylpropyl)tricyclo(5.2.1.0<2,6>)dec-8-ene-3,5-dione or a pharmaceutically acceptable salt thereof; 4-{1-methyl-1-((2,4,6-trimethoxyphenyl)methylthio)ethyl}-1,3-oxazolidin-2-one or a pharmaceutically acceptable salt thereof; and 2-amino-3-methyl-3-((2,4,6-trimethoxyphenyl)methylthio)butan-1-ol or a pharmaceutically acceptable salt thereof.

28. 4-aza-4-(2-methyl-2-(nitrosothio)propyl)tricyclo(5.2.1.0<2,6>)dec-8-ene-3,5-dione or a pharmaceutically acceptable salt thereof.

29. 4-(1-methyl-1-(nitrosothio)ethyl)-1,3-oxazolidin-2-one or a pharmaceutically acceptable salt thereof.